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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,141	07/02/2007	Mara Rossi	ROSSI 10	1796

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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,141	ROSSI ET AL.	
	Examiner	Art Unit	
	JEGATHEESAN SEHARASEYON	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2012*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-3 and 5-9* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-3 and 5-9* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/25/11 and 1/18/12*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is in response to Applicant's remarks filed 1/18/12. Claim 9 is newly added. Thus, claims 1-3 and 5-9 are pending and examined.

Information Disclosure Statement

2. The information disclosure statement(s) filed 10/25/11 and 1/18/12 have been considered.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. The rejection of claims 1-3, 5-8 and 9 (newly added) under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for the recovery of chemokine of SEQ IDNO: 1, does not reasonably provide enablement for recovering all chemokine molecules expressed in prokaryotic host cells as inclusion bodies is maintained for reasons set forth in the Office Action dated 10/18/11.

Applicant asserts that the chemokines are known to share numerous features, such as the presence at conserved positions of cysteine residues forming disulfide bonds, conserved amino acid structures, similar 3-D structures, short N-term chains and long C-term chains, receptor binding via N-term chains. It is asserted that the chemokine of SEQ ID NO: 1 conserves the basic amino acid structure of C-C chemokines, i.e. -C-C-X_{22-23}-C-X_{15}-C-. Applicant claims that this mutant still binds the CCR5 receptor similar to the wild type RANTES protein. Applicant further claims that it

would be recognized and understood by one of skill in the art that such similar binding implies that the three dimensional conformation of the wild type protein is maintained in the mutant protein, and therefore it has a similar structure/conformation to wild-type RANTES, as well as to other chemokines. Applicant asserts that because of the many similarities/correlations, with regard to the structure/confirmation, between the different types of chemokines, as established in the prior art, one of skill in the art would have no doubt that they could purify any chemokine according to the presently claimed method based on the guidance of a single working example for a triple RANTES mutant in the present specification. In addition, it is asserted a person would have a reasonable expectation that the presently claimed process can be applied to the recovery of any chemokine expressed in prokaryotic host cells as inclusion bodies. Thus, Applicant asserts that there is sufficient enabling disclosure to extend the presently claimed process to other chemokines. Applicant contends that due to the similarities/correlations between the different chemokines, which is well known in the art as discussed above, the single working example with a triple RANTES mutant in the present specification is sufficient to provide guidance that enables one of skill in the art to extend the presently claimed process to other chemokines. Applicant is also asserting that there is no requirement that every possible embodiment of a claim be supported by a working example.

Applicant's arguments have been fully considered but are not found to be persuasive. Although, as indicated by the Applicant there is considerable structural similarities between chemokine proteins, Clore et al. disclose the following structural

differences between IL-8 and hMIP-1β at the monomer level (p. 58). The reference teaches that the confirmation of the first disulfide bridge is a right handed hook in IL-8 as opposed to a left-handed spiral in hMIP-1β. Clore et al. disclose that that this associated with the insertion in IL-8 of a residue between the first two cysteines and of two residues in the turn connecting β-strands 1 and 2. It teaches that the second disulfide bridge is almost perfectly superimposable between the two structures. The reference further teaches that the helix extends for five residues further at the C-terminus in IL-8 compared to hMIP-1β. The reference also discloses the confirmation of the turn connecting strands β_2 and β_3 differs around residues 46 and 47 (residue number of hMIP-1β). Clore et al. disclose that the direction of the N-terminal residues preceding the first cysteine is completely different. In addition, members within each subfamily exhibit 25-70% sequence identity, while the amino acid identity between members of the two subfamilies ranges from 20 to 40% (p.57). Clore et al. disclose that apart from backbone hydrogen bonding, all the interactions that stabilize the dimer in hMIP-1β are hydrophobic in nature, and all but one, consisting of a potential single salt bridge, are hydrophobic in IL-8 ((p.59). Similarly, Baggiolini et al. (1994, IDS of 1/18/12) reference also disclose the sequence variability between chemokines (Figure 1 and Table 1). Further, the handbook of analysis and purification of peptides and proteins by reversed-phase HPLC discloses that RP-HPLC separates polypeptides based on subtle differences in the "hydrophobic foot" of the polypeptide being separated (p.4). Differences in the "hydrophobic foot" result from differences in amino acid sequences and differences in confirmation (p.4). Therefore, based on the prior art teachings a

person would not have a reasonable expectation that the presently claimed process can be applied to the recovery of any chemokine expressed in prokaryotic host cells as inclusion bodies because although the chemokines in general have structural similarity they do have considerable sequence variability, charge and hydrophobicity. Although, there is no requirement that every possible embodiment of a claim be supported by a working example, in the instant invention the specification (provides a single chemokine) and prior art does not provide adequate guidance. Thus, due to the excessive breadth of the claims, which read on recovery of all chemokines, the lack of guidance and examples in the specification and prior art, and the unpredictability inherent invention regarding the purification of chemokines, a person of ordinary skill in the art would require further, undue experimentation to determine the chemokines that can be purified by interposing Reverse Phase Chromatography step.

3b. The rejection of claims 1-3, 5-8 and 9 (newly added) under 35 U.S.C. 112, first paragraph, as containing subject matter which not described in the specification in such a way as to reasonably convey to one skilled in the art that that the inventors at the time the application was filed, had possession of the instant invention is for reasons set forth in the Office Action dated 10/18/11.

Applicant is arguing as in paragraph 3a that there is no requirement to describe every chemokine useful in the process according to the present invention in order to show possession of the claimed invention. Applicant is asserting that in accordance MPEP, applicants did not describe every chemokine known in the art but rather cited references in the specification that provide disclosure and teachings of the well-known

genus of chemokines (i.e., C-C, C-X-C and C-X_3-C chemokines) which the triple RANTES is representative of based on similarity in structure/conformation. Applicant is also noting that they are not claiming a product but rather a method for recovering chemokines, a group which were well known in the art at the time the invention was made and which are structurally very similar.

Applicant's arguments have been fully considered but are not found to be persuasive. While it is true that the Applicant has provided references to indicate that there is structural similarity between chemokines, the prior art also teaches that there is considerable sequence diversity between the chmiokines (see Baggiolini et al. and Clore et al.). Since, the handbook of analysis and purification of peptides and proteins by reversed-phase HPLC discloses that RP-HPLC separates polypeptides based on subtle differences in the "hydrophobic foot" of the polypeptide being separated, there is inadequate written description support for the instant invention. In addition, M.P.E.P § 2163 [R-5] state that "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., Moba, B.V. v. Diamond Automation, Inc., 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116". There is no identification of any chemokine other than RANTES of SEQ ID NO: 1. There is no disclosure of other chemokine of SEQ ID NO: 1. Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus.

Conclusion

4. No claims are allowed. However, if limitation of claim 1 is incorporated into claim 5, it will be allowable.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEGATHEESAN SEHARASEYON whose telephone number is (571)272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph. D can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christine J Saoud/
Primary Examiner, Art Unit 1647

JS
3/17/12